



Global Pediatric Development: Comparison of PSP and PIP

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Brief Glossary

- PREA: Pediatric Research Equity Act
- BPCA: Best Pharmaceuticals for Children Act
- PeRC: Pediatric Review Committee
- PSP: Pediatric Study Plan
- PIP: Pediatric Investigation Plan
- EMA: European Medicines Agency
- PDCO: Paediatric Committee

PREA and BPCA

- **Pediatric Research Equity Act (PREA)**
 - **Requires** companies to assess safety and effectiveness of new drugs/biologics in pediatric patients (Pediatric Assessment)
- **Best Pharmaceuticals for Children Act (BPCA)**
 - **Provides a financial incentive** to companies to voluntarily conduct pediatric studies

PREA vs. BPCA

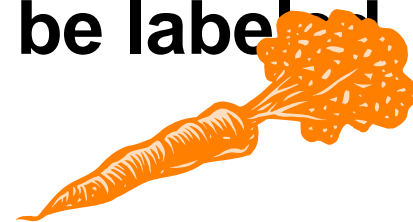
PREA

- ☐ Drugs and biologics
- ☐ **Mandatory** studies
- ☐ Requires studies **only on indication(s) under review**
- ☐ **Orphan indications exempt** from studies
- ☐ Pediatric studies must be labeled



BPCA

- ☐ Drugs and biologics
- ☐ **Voluntary** studies
- ☐ Studies relate to entire moiety and **may expand indications**
- ☐ Studies may be requested for orphan indications
- ☐ Pediatric studies must be labeled



Pediatric Review Committee (PeRC)

- Established by legislation to carry out the activities described under PREA and BPCA
- Intended to increase the consistency of implementation of provisions of PREA and BPCA across FDA
- Committee membership
 - Expertise in Pediatrics, Neonatology, Pediatric Ethics, Biopharmacology, Statistics, Chemistry, Law required
 - Appropriate expertise pertaining to the product under review

Brief History of PSP

- Requirement under PREA as amended by FDASIA (Section 506)
 - FDA encourages inclusion of all pediatric plans including those plans as may be studied under BPCA (i.e., under WR)
- Encourage sponsors to identify pediatric studies as early as possible in product development
- When appropriate, conduct pediatric studies prior to the submission of the NDA or BLA
- Implemented January, 2013
 - 292 Initial PSPs received
 - 193 Initial PSPs reviewed
 - 74 Agreed initial PSPs

PSP: Goals of Pediatric Development

- Obtain sufficient data to support the dosing, safety and efficacy in the pediatric population
- Communicate that data in the product labeling
- Judicious use of medication in the pediatric population

Contents of PSP

- Overview of Disease and Overview of Product
- Plan for Extrapolation
- Plans for requests for Waivers
- Summary of Planned clinical and nonclinical studies
- Formulation development
- Nonclinical studies
- Clinical data to support planned studies
- Planned clinical studies
- Timeline
- Plans for request for Deferrals
- Agreements with other Regulatory Authorities
- **Guidance suggests no more than 60 pages total**

European Medicines Agency

- EMA coordinates member states activities with respect to medicines
- Single application to the EMA to obtain marketing authorization in all EU member states

How is the EMA organised?

**33+ National Competent
Authorities
+ 3000 European experts**

**EU institutions:
Commission - Parliament**

Management Board

**Committee for Herbal
Medicinal Products**

**Committee for Veterinary
Medicinal Products**

**Committee for
Advanced Therapies (CAT)**

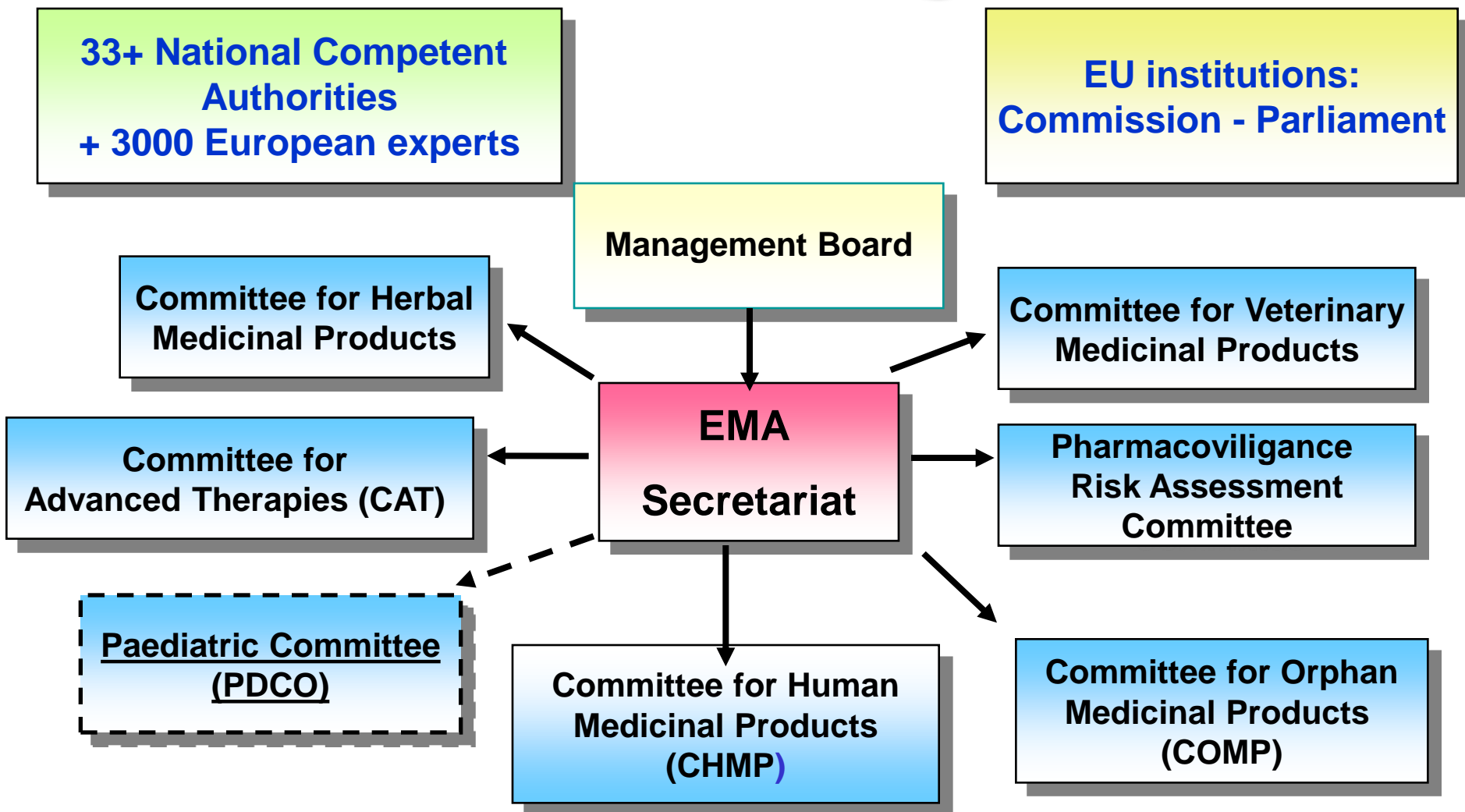
**EMA
Secretariat**

**Pharmacovigilance
Risk Assessment
Committee**

**Paediatric Committee
(PDCO)**

**Committee for Human
Medicinal Products
(CHMP)**

**Committee for Orphan
Medicinal Products
(COMP)**



Brief History of PIP

- Pediatric Regulation instituted in EU January, 2007
 - Established the PDCO
 - Required submission of a PIP at filing
- Encourage sponsors to identify pediatric studies as in product development
- Five year report published
 - 600 PIPs agreed upon
 - 453 for products not yet authorized in EU
 - 147 for products already authorized (new indication)

PIP: Goals of Pediatric Development

- Ensure that the necessary data are obtained in children, when safe to do so
- Support the authorization of a medicine for children

Contents of PIP

- Description of studies and measures to adapt the medicine's formulation so that acceptable in children
- Cover the needs of all age groups (birth to adolescents)
- Define the timing of studies in children compared to adults
 - Studies may be deferred and/or waived as appropriate

Note: PIP may be modified

PIP Application Summary

- Active substance(s), class and mechanism of action
- Product Name
- MAH/applicant
- Planned indication(s) in adults
- Condition
- Proposed indication(s) in children
- Potential benefit for children
- Clinical development
- Pharmaceutical form
- Nonclinical plans
- Extrapolation
- Waiver (s), deferrals

Contents of PIP

- Part A: Administrative and product information
- Part B: Overall development of the medicinal product including information on the conditions
- Part C: Applications for product specific waivers
- Part D: Paediatric investigation plan
- Part E: Applications for deferrals
- Part F: Annexes
- EMA website suggests that Parts B-E should be limited to 50 pages or less

Similarities

- Goal of each program is the same
- Scientific elements of PSP and PIP are consistent
 - Descriptions of product, disease and alternative treatments
 - Plans for requesting waivers, deferrals and developing pediatric formulations
 - Need for nonclinical studies
 - Timing of studies and role of extrapolation

Comparison: PSP and PIP

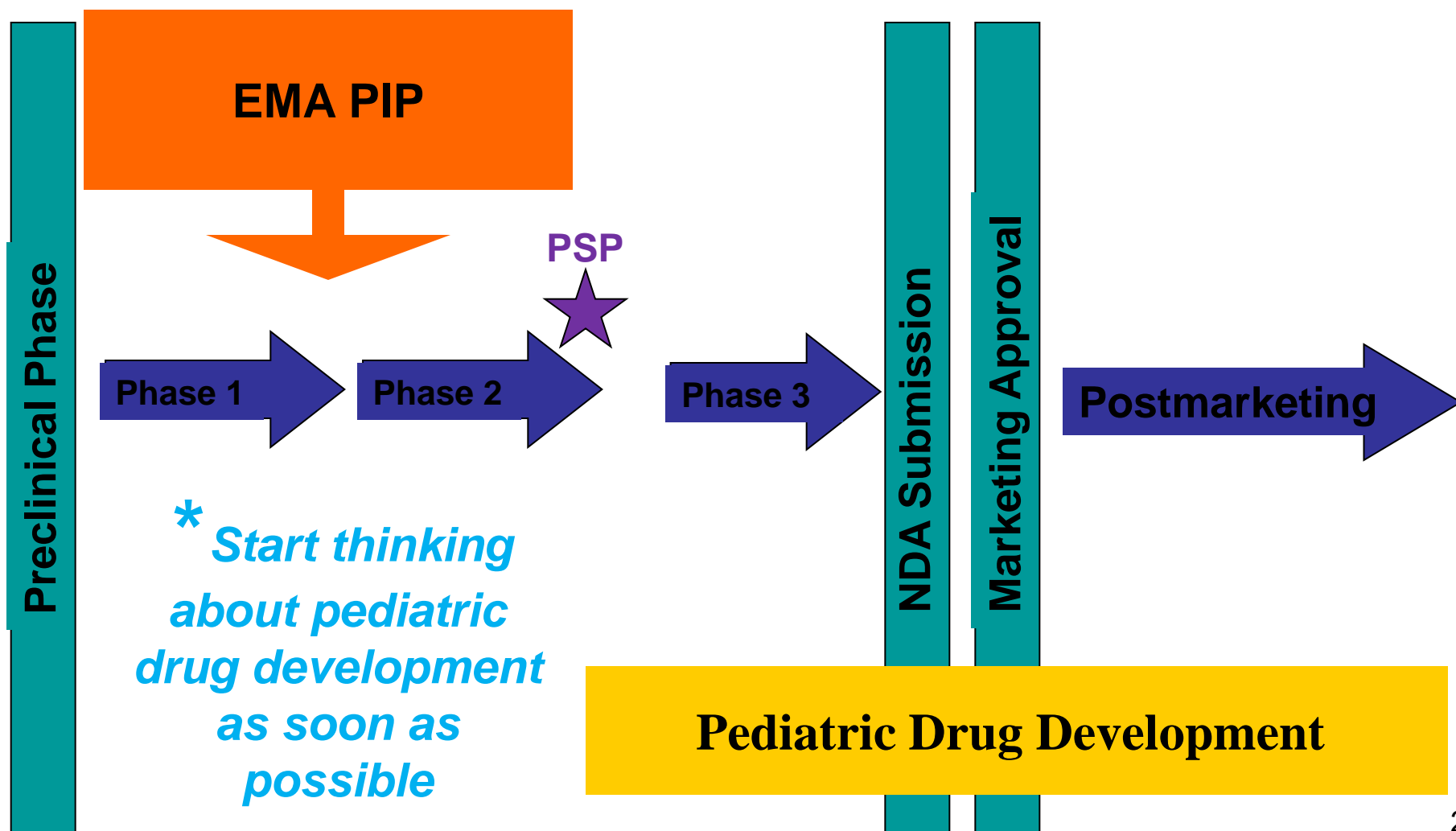
Part B- Overall development of the medicinal product	B. and B.1.1-2 Discussion on similarities and differences of the disease/condition between populations and pharmacological rationale	1. Overview of Disease/ Condition in the Pediatric Population 2. Overview of Drug or Biological Product 3. Overview of Extrapolation
	B.2. Current methods of diagnosis/prevention/treatment	1. Overview of the Disease Condition in Pediatric Population
	B.3. Significant therapeutic benefit /fulfilment of need	2. Overview of the Drug or Biological Product(s)
Part C- Applications for product-specific waivers	C.1.and C.2.1-3 Waiver overview and grounds for product waiver	4. Request for Drug-Specific Waiver(s)
Part E -Applications for deferral	Part E Applications for deferral	11. Plan to Request Deferral
		12. Agreements for Other Pediatric Studies
		VI. Contents of Requested Amendment to Initial PSP

Part D Paediatric investigation plan	D.1. Existing data and overall strategy for development	8. Clinical Data to Support Pediatric Studies
	D.1.1. PIP indication	2. Overview of the Drug or Biological Product.
	D.1.2. Paediatric subset(s)	11. Plan to Request Deferral
	D.1.3. Information on existing quality/ non-clinical/clinical data Address need to demonstrate efficacy or extrapolate efficacy	8. Clinical Data to Support Studies in Pediatric Patients Overview of Planned Extrapolation
	D.2. and D.2.1 Quality aspects	6. Pediatric Formulation Development
	D.2.2. Outline of planned/ongoing studies and steps in the pharmaceutical development	5. Summary of Planned Nonclinical and Clinical Studies 6. Pediatric Formulation Development
	D.3., D.3.1-3 Non-clinical aspects and planned/ongoing studies, including study(ies) summary	5. Summary of Planned Nonclinical Studies and 7. Nonclinical Studies
	D.4, D.4.1-3. Clinical aspects and planned/ongoing studies, including study(ies) summary; list key elements of modeling/ simulation and extrapolation	5. Summary of Planned Clinical Studies 9. and 9.1-2 Planned Pediatric Studies: PK and efficacy/ safety

Important Differences

- Regulatory requirements
 - distinct incentive (BPCA) and requirement (PREA) programs in US; combined incentive and requirement program in EU (PIP)
 - focus on indication (PREA) vs. condition (PIP)
- Review processes and timelines in each agency

Pediatric Drug Development Plans: alignment with the adult drug development process



Conclusions

- Goal of each program is the same
 - Sound and efficient global pediatric development
- Scientific elements of PSP and PIP are consistent
- Process to encourage consistent scientific advice (EMA cluster calls)

Resources

- PSP

Guidance for Industry: Pediatric Study Plans

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM360507.Pdf>

- PIP

Pediatric investigation plans, waivers and modifications

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000293.jsp&mid=WC0b01ac0580025b91